UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

NOV 17 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: PP#2F2632. Acephate on Peanuts. Amendment of 9/28/82.

From: Martha J. Bradley, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Thru: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

To: William Miller PM 16
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Chevron Chemical Company has submitted a revised label which includes a livestock feeding and grazing restriction for peanut hay as well as peanut forage in response to our (N. Whetzel) memo of 8/23/82.

The remaining feed items in this petition are peanut meal at 0.2 ppm and peanut hulls at 5 ppm. Feeding of these commodities to livestock will not result in any additional dietary intake of residues because these feed items would be fed instead of items such as cottonseed and soybean meal which have higher tolerance levels.

We conclude that the established meat and milk tolerances are adequate for the peanut feed items.

We note that several petitions with livestock feed items that may require higher meat and milk tolerances are pending.

No other RCB deficiencies remain in this petition; therefore, we now recommend for the establishment of the proposed tolerances provided TOX concurs.

TS-769:RCB:MBradley:CM#2:Rm810:X77377:11/17/82
cc: RF, Circ., Perfetti, Thompson, FDA, TOX, EEB, PP#2F2632
RDI: Onley, 11/12/82; Schmitt, 11/12/82

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 23 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#2F2632 Acephate on Peanuts. Evaluation of analytical method and residue data.

FROM: N. K. Whetzel, Chemist
Residue Chemistry Branch, HED (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch (TS-769)

TO: W. H. Miller, Product Manager No. 16
Registration Division (TS-767)
and
Toxicology Branch (TS-769)
Hazard Evaluation Division

The Chevron Chemical Company proposes tolerances for residues of the insecticide acephate (O,S-dimethyl acetylphosphoramidothioate), and its cholinesterase-inhibiting metabolite (O,S-dimethyl phosphoramidothioate; methamidophos) in or on peanuts at 0.2 ppm and peanut hulls at 5 ppm.

Tolerances are established (40 CFR 180.108) for combined residues of acephate and its cholinesterase-inhibiting metabolite methamidophos in or on mint hay (15 ppm - maximum 1 ppm methamidophos), lettuce and celery (10 ppm-maximum 1 ppm methamidophos), bell peppers (4 ppm - maximum 1 ppm methamidophos), dry and succlent beans (3 ppm - maximum 1 ppm methamidophos), cottonseed (2 ppm), soybeans (1 ppm), and 0.1 ppm in eggs, milk, meat, fat, and meat by-products of livestock.

Food additive tolerances are established for combined residues of acephate and methamidophos in or on cottonseed meal (8 ppm), and cottonseed hulls and soybean meal (4 ppm).

Conclusions

1. The nature of the residue in plants and animals is adequately delineated.

2. Adequate analytical methods are available for enforcement of the proposed tolerances.

3a. Residues in peanut meats are not likely to exceed the proposed 0.2 ppm tolerance.

3b. Residues in peanut hulls are not likely to exceed the proposed 5 ppm tolerance from the proposed use.

3c. Since residues in peanut meal and oil were less than the maximum residues in peanut meats, there will be no need to proposed food additive tolerances on these commodities.

3d. The petitioner will need to propose a label restriction on peanut hay or propose a tolerance for acephate on peanut hay.

4a. There will be no problem of secondary residues in poultry, and eggs which will cause the established tolerances to be exceeded.

4b. We reserve our conclusion on the adequacy of the established tolerances on meat and milk until we know the petitioner's intent with regard to peanut hay (see conclusion 3d, above).

5. Presently, No CODEX, Canadian and Mexican tolerances for acephate on peanuts have been established; an International Residue Limit Status sheet is attached.

Recommendations: RCB recommends against the establishment of the proposed tolerances because of Conclusions 3d and 4b above.

## Detailed Considerations

### Manufacture and Formulation

Acephate is formulated as Orthene® 75S, a soluble powder containing 75 percent active ingredient, for use as a foliar spray on peanuts.

The inert ingredients in the formulation are cleared for use under §180.1001.

The manufacturing process for technical acephate is included in PP#2G1248. Technical acephate contains 88-96% acephate. The impurities are not likely to be a residue problem.

### Proposed Use

Multiple ground or aerial applications at 0.25-1.0 lb ai/A may be made; they are started when insects first appear and repeated as necessary. Do not apply within 14 days of digging. Do not feed treated forage to livestock or allow animals to graze treated areas.

The petitioner will need to propose a label restriction on peanut hay or proposed a tolerance for acephate on peanut hay.

### Nature of the Residue

The metabolism of acephate in animals (cows, goats, swine, poultry) and plants (beans, cabbage, tomatoes, radishes, alfalfa) has been fully discussed in PPs 2G1248 and 3F1375. The significant components of the residues of both animals and plants is the parent compound acephate and its cholinesterase-inhibiting metabolite methamidophos.

The nature of the residue in plants and animals is adequately delineated.

Analytical Method

The method used in this petition determines both acephate and methamidophos. Briefly, the macerated sample is extracted with hexane/acetonitrile. The hexane is discarded and the acetonitrile is removed by rotary evaporation. The residue is cleaned up on a silica gel column using ethyl ether/methanol for elution. Residue determinations are made by gas chromatography incorporating a thermionic detector.

Shelled peanuts fortified with 0.25 ppm acephate gave an average recovery of 91% (range 75-108%). When samples were fortified with 0.1 ppm methamidiphos the average recovery was 90% (range 70-109%). Acephate recovery values for other plant parts and processing fractions have also been submitted.

Control values for nuts were consistantly <0.02 ppm. For hay and forage control values as high as 0.27 ppm are reported. The validated sensitivity for this method (as reported in PAM II) is 0.01 ppm for acephate and 0.04 ppm for methamidiphos.

We conclude that adequate analytical methods are available for enforcement purposes.

Residue Data

Residue experiments were carried out in Alabama, Florida, Georgia, North Carolina, Virginia, Oklahoma, and Texas. Application rates ranged from 0.5 lb ai/A to 2.0 lb ai/A; 1 to 8 applications were made. PHI's ranged from 0 to 54 days.

The highest combined residues found in peanuts (shelled nuts) resulting from the proposed rate and a 2X rate was 0.09 ppm (of which 0.02 ppm was methamidophos). This residue (0.09 ppm) resulted from the proposed rate (1.0 lb ai/A) and a a 52 day PHI; the proposed PHI is 14 days. In most instances no residue was found in the peanuts.

With regard to processed peanut fractions, no residues were detected in the oil; only one combined residue of 0.08 ppm (0.03 ppm of which was methamidophos) was found in meal treated with 3 applications, the first at 0.75 lb ai/A and the last 2 at 1.0 lb ai/A (maximum application rate) at 14 days PHI.

The combined residue values reported for peanut hulls as a result of 1-4 applications of the maximum proposed rate (1 lb. a.i./A) ranged from 0.00-3.0 ppm at PHI's from 13-52 days. The highest residue found resulted from 3 applications and a PHI of 52 days. From a 2X the application (1-4 applications, 13-46 day PHI's) rate, combined residues on hulls ranged from 0.00-1.7 ppm.

In peanut hay, combined residues resulting from 1-3 applications at the maximum proposed rate and 13-21 day PHIs, ranged from 1.1-20 ppm. The highest residue was obtained from 2 applications at 14 days PHI. Combined

residues resulting from a 2X application rate ranged from 2.7-19 ppm (1-4 applications and 14-21 day PHIs). The maximum residue (19 ppm) resulted from 1 application at 21 days PHI.

The maximum residue found was 25 ppm; this residue resulted from 8 applications at the 0.75 lb ai/A rate and a 0 day PHI.

In peanut forage, combined residues ranged from 3.3-34 ppm from the maximum proposed rate. These resulted from 1-4 applications and 11-15 day PHIs. The maximum residue was the result of 1 application and an 11 day PHI. At 2X the maximum rate used, combined residues ranged from 1.2-66 ppm under the same conditions as at the 1X rate. The highest residue resulted from 1 application and a 11 day PHI.

We conclude that residues of acephate and methamidophos in/on peanuts and peanut hulls will not exceed the proposed tolerances from the proposed use.

Since none of the residues in oil and meal exceeded the residues found in peanut meats (shelled nuts), we do not expect residues in peanut meal or oil. We conclude that no food additive tolerances are needed for peanut meal and oil.

Meat, Milk, Poultry, and Eggs

Peanuts, peanut hulls, peanut vines, forage and hay, and peanut meal are the feed items of concern. The petitioner has proposed grazing and feeding restrictions. However, he will either have to propose a hay feeding restriction or propose a tolerance on peanut hay. Therefore, we reserve our conclusion on the adequacy of the established tolerances on meat and milk until we know the petitioner's intent with regard to peanut hay.

We conclude that secondary residues in poultry, and eggs will not exceed the established tolerances from the proposed use.

cc: R.F.
Circu
Reviewer
FDA
PP# No. 2F2632
TOX
EEB
EFB
Robert E. Thompson (Res. Triangle Park, NC)
RDI:Section Head:(Acting)JHO:Date:8/10/82:RDS:Date:8/10/82
TS-769:RCB:Reviewer:NKWhetzel:LDT:X77324:NKW:Date:8/4/82:CM#2:RM:815

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Toxicology Branch/HED Review

RCB Anne Filepetition

Caswell No(s).: 2A

To: Mr. W.H. Miller/Ms. M.A. Mautz, P.M. Team 16, RD/IRB (TS-767)

Registration No(s).: 239-2418

Pesticide Petition No(s).: 2F 2632

Chemical(s): O,S-Dimethyl acetylphosphoramidothioate (acephate), formulated as Orthene 75 S Soluble Powder (Orthene 75 S); a.i. = 75 %

Requested Action(s): Amended registration to add peanuts to 239-2418 (Orthene 75 S). Proposed tolerances: Shelled peanuts, 0.2 ppm and peanut hulls, 5 ppm.

Recommendation: Conditional registration is recommended, provided RCB supports the proposed residue levels (RCB has not yet reviewed this action). Peanut oil contains no acephate. Peanut meal contains 0.08 ppm of acephate, which is less than the tolerance

Inert(s) cleared 180.1001: Yes; required for peanuts (raw agric. commodity).

% of ADI occupied: Existing: 30.35 Resulting: 30.43

Resulting % increase in TMRC: 0.24

Data considered in setting the ADI: 28-month rat feeding/oncogenic study. The NOEL = 5 ppm (0.25 mg/kg), based on the inhibition of RBC, plasma and brain cholinesterase activiti

Attached (?): ADI printout: (YES) NO; TOX "one-liner": YES (NO); DER: (YES) NO

Existing regulatory actions against registration: NO

RPAR status: NO

New Data: NO

Data gaps: Please see attachment.

Comments: Adequate toxicity data are available to support conditionally this very small increase in TMRC (conditionally, because toxicity data gaps still exist). The PHI will be 14 days. Secondary residues in meat and milk will be covered by the already established tolerances (0.1 ppm) for acephate in these products. Furthermore, most peanuts are roasted before being consumed by people and heat treatment, like roasting, reduces or eliminates acephate residues in peanuts.

Reviewer: Ruptyya K. Loche 5/21/82 Date: MAY 24 1982

Section Head: [signature] 5/21/82 Branch Chief: [signature] 5/24/82

CFR 180.108 Acephate 5/21/82

Verified Printout

NOEL change not received

ACCEPTABLE DAILY INTAKE DATA

| RAT, Older | NOEL mg/kg | NOEL ppm * | S.F. | ADI mg/kg/day | MPI mg/day/60kg |
|---|---|---|---|---|---|
| | 0.250 | 5.00 | 10 | 0.0250 | 1.5000 |

Published Tolerances

| CROP | Tolerance | Food Factor | mg/day/1.5kg |
|---|---|---|---|
| Celery( 28) | 10.000 | 0.29 | 0.04292 |
| Lettuce( 84) | 10.000 | 1.31 | 0.19622 |
| Peppers(120) | 4.000 | 0.12 | 0.00736 |
| Beans( 9) | 3.000 | 2.04 | 0.09180 |
| Cottonseed (oil)( 41) | 2.000 | 0.15 | 0.00450 |
| Soybeans (oil)(148) | 1.000 | 0.92 | 0.01377 |
| Eggs( 54) | 0.100 | 2.77 | 0.00416 |
| Milk&Dairy Products( 95) | 0.100 | 28.62 | 0.04292 |
| Meat,inc poultry( 89) | 0.100 | 13.85 | 0.02077 |

| MPI | TMRC | % ADI |
|---|---|---|
| 1.5000 mg/day/60kg | 0.4244 mg/day/1.5kg | 28.29 |

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Unpublished, Tox Approved 1G2550, 9H5216

| CROP | Tolerance | Food Factor | mg/day/1.5kg |
|---|---|---|---|
| Avocados( 6) | 2.000 | 0.03 | 0.00090 |
| All foods(197) | 0.020 | 100.00 | 0.03000 |

| MPI | TMRC | % ADI |
|---|---|---|
| 1.5000 mg/day/60kg | 0.4553 mg/day/1.5kg | 30.35 |

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Current Action 2F2632

| CROP | Tolerance | Food Factor | mg/day/1.5kg |
|---|---|---|---|
| Peanuts(115) | 0.200 | 0.36 | 0.00107 |

| MPI | TMRC | % ADI |
|---|---|---|
| 1.5000 mg/day/60kg | 0.4564 mg/day/1.5kg | 30.43 |

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$\frac{0.0011 \times 100}{0.4564} = 0.24\%$ (increase in TMRC due to current action)

* Although this has not yet been finalized, it is anticipated that the NOEL for acephate will be 5 ppm (0.25 mg/kg). This value is based on the inhibition of cholinesterase activity in plasma, erythrocytes and brain (28-month rat feeding study). Using this NOEL and the safety factor of 10, the ADI (MPI) = 1.5 mg/day/60 kg person.

Existing Toxicity Data Bank for Acephate:

Acephate is currently undergoing an active Registration Standards Review. The toxicity data baseline, derived from that review, is as follows:

| Study | Results | Core (Other) Grade |
|---|---|---|
| Acute Delayed Neurotoxicity (hen) | Not observed (no leg paralysis) at the 375 mg/kg level. | Supplementary |
| Subchronic (90-day) feeding: cholinesterase activity (rat) | NOEL = 5 ppm (0.25 mg/kg), based on the inhibition of cholinesterase activity in plasma, RBC and brain; M+F | Minimum |
| Subchronic (37-73 days) oral dosing (human) | NOEL = 0.02 mg Monitor + 0.18 mg Acephate/kg (M) and 0.03 mg Monitor + 0.27 mg Acephate/kg (F), based on the inhibition of plasma cholinesterase activity and systemic effects. | Acceptable as Supplementary Data |
| Chronic (2-year) feeding (dog) | NOEL = 30 ppm (0.75 mg/kg), based on the inhibition of plasma, RBC and brain cholinesterase activity; M & F. NOEL = > 100 ppm (2.5 mg/kg), for systemic toxicity; M+F. | Minimum |
| Chronic 28-months) feeding/oncogenic (rat) | NOEL = 5 ppm (0.25 mg/kg), based on the inhibition of cholinesterase activity in plasma, RBC and brain; M+F (Not yet finalized). | Minimum for the chronic feeding part and Supplementary for the oncogenic part. |
| Oncogenic: Interim Report (mouse) | Incomplete data | Supplementary |
| Teratogenic (rabbit) | Not fetotoxic or teratogenic at the 10 mg/kg (highest tested). Slight maternal toxicity was observed at this level. | Minimum |

| | | |
|---|---|---|
| | teratogenic at the g/kg level (highest ) Slight maternal y was observed at vel. | Minimum |
| | ate is capable of cing point mutations can damage DNA in east cells, mammalian cells in culture and human cells in culture. No chromosomal effects were found. | Acceptable |
| (rat) | Acephate was excreted essentially unchanged in urine, in 6 hours after dosing. Did not accumulate in tissues and was not converted to Monitor. | Minimum |
| Reproduction | Study is still missing as far as the Agency is concerned. According to Chevron Chemical Company, this study was just completed (March, 1982) in England. | |

Studies with Orthene 75 S Soluble Powder (Orthene 75 S)

| Study | Results | Toxicity Category | Core (Other Grade |
|---|---|---|---|
| Acute Oral LD50, (rabbit)* | LD50 = 707 mg/kg; M | - | Acceptable |
| Acute Dermal LD50, (rabbit) | LD50 = > 10 g/kg; M+F | IV | Minimum |
| Acute Inhalation LC50 (rat) | LC50 = > 12.1 mg/l; M+F | III | Minimum |
| Primary Dermal Irritation (rabbit) | PIS = 0 | IV | Minimum |
| Primary Eye Irritation (rabbit) | No irritation on day 7. | III | Minimum |
| Dermal Sensitization (rabbit) | Not a sensitizer. Scores for days 1 thru 16 were 0-0.8. Challenge score (Draize) was 0.25. | - | Minimum |

* There is no acute oral LD50 rat study with Orthene 75 S, containing 75% acephate. The following values were obtained in an acute oral LD50 study with Orthene 85, a formulation containing 85% acephate: LD50 = 1490 mg/kg (male rat) and LD50 = 739 mg/kg (female rat).

# TOXICITY DATA GAPS FOR ACEPHATE

The following studies are either missing or are incomplete (supplementary) and require replacement:

| Study | Missing | Supplementary |
|---|---|---|
| Dermal Sensitization | | ✓ |
| Acute Delayed Neurotoxicity | | ✓ |
| 21-Day Dermal | ✓ | |
| Oncogenic (mouse) | | ✓ |
| Oncogenic (rat) | | ✓ |
| Reproduction | ✓ | |
| Mutagenic | | ✓ |

13544

# R104094

| | |
|---|---|
| **Chemical:** | **Acephate** |
| **PC Code:** | **103301** |
| **HED File Code** | **11500 Petition Files Chemistry** |
| **Memo Date:** | **12/09/2004** |
| **File ID:** | **00000000** |
| **Accession Number:** | **412-05-0088** |

**HED Records Reference Center**
**01/07/2005**